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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/628,225	07/28/2000	William W. Bachovchin	TUU-P01-006	3405

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1654	21

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/628,225	BACHOVCHIN ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14,16* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *20* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The response filed July 24, 2002 did not include claims 44 and 45 in the listing of all claims being examined, nor was there any amendment instruction requesting cancellation of claims 44 and 45. Accordingly, claims 44 and 45 as presented in the amendment filed November 30, 2001 are deemed to be pending in this application.

The response filed November 30, 2001 did not accurately mark all amendments to the claims as required by 37 CFR 1.121(c)(1). In particular, the clean copy of claim 38 begins with a lower-case "a" rather than the upper-case "A" which begins the marked-up copy of the claim. The clean copy of amended claim 66 permits W to be -CN, whereas in the marked-up copy this possibility is deleted. Any future amendments to the claims should be carefully checked to ensure accurate marking of all amendments to the claims as required by 37 CFR 1.121.

2. The declaration signed by Inventor Bachovchin filed July 24, 2002 is approved.

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 and/or 120 as follows:

The claim for priority inserted by the amendment filed July 24, 2002 is objected to because a provisional application can not claim priority based upon any other type of application, and because an application can not claim priority based upon a later-filed application. The claim for priority inserted by the preliminary amendment filed July 24, 2002 is objected to because there is no copendency between the U.S. Provisional Application and the instant application. Finally, the claim for priority inserted by the preliminary amendment filed July 24, 2002 is objected to because it is not the first sentence of the specification. See MPEP 310.

Correction is required.

It appears that the order of the applications upon which priority is claimed has been inverted. Concerning copendency, while there could be copendency with the PCT application based upon its entry into Chapter II, there is no copendency with the immediate parent application as set forth in the current claim for priority. Concerning the location of the claim for priority, the claim for priority has still not been inserted as the first sentence of the specification, i.e. before the Funding section.

Once an appropriate claim for priority under 35 U.S.C. 120 and 119(e) is presented, it would appear that instant claims 38-41 and 43-67 would be entitled under 35 U.S.C. 120 and 119(e) to the benefit of the filing date of provisional application 60/073,409 because the '409 application, under the test of 35 U.S.C. 112, first paragraph, discloses the claimed invention.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure of the cause of the glucose intolerance recited in instant claim 42. Applicants cite to page 51, line 6, of the specification as support for the amended claim limitation. However, the examiner has not been able to locate a copy of the cited article in order to determine whether or not it supports the claim limitation. (Applicants are requested to check the citation for this article, because the journal "Gastroenterology" lists Volumes 112 and 113, rather than Volume 35, as occurring in 1997.) Further, the citation in the specification is limited to mice, and there is no indication that a GLP-

1 receptor gene deletion or disruption exists in glucose intolerant animals in general. Finally, it is not clear, from the brief summary of the article given in the specification, that the article supports both deletion and disruption of the gene encoding the receptor. In general, disclosure of a species (e.g., just mice, or just gene deletion, or just gene disruption) does not constitute adequate written descriptive support for newly presented claims drawn to a genus encompassing the species.

6. Claims 38-49 and 51-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a K_i in the nanomolar range" in claims 38-40 is indefinite because it is not clear what upper limit is intended for this range. It is not clear, e.g., if the upper limit of this range is about 1 nanomolar, if single digit nanomolar values are embraced, or if double-digit nanomolar values are embraced. All these values are commonly expressed in terms of nanomolars, but the specification at page 6, lines 9-13, implies that only the more limiting range may be intended by Applicants. There is no antecedent basis in the claims for the phrase "the glucagon type peptide" in claim 43. Note that claim 42 recites a glucagon type peptide 1 receptor, not a peptide and not a GLP in general. Claim 66 is indefinite because it defines a variable R_1 which is not used in any of the chemical structures found in the claim.

7. Claims 38 and 65 are objected to because of the following informalities: At claim 38, line 1, "a" (first occurrence) should be capitalized. At claim 65 (page 15, line 13), "or" should be inserted before the last chemical structure in the line. Appropriate correction is required.

8. Claims 44 and 45 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to

cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 44 is of identical scope as independent claim 38, which already requires the inhibition of DPIV-mediated proteolysis. Claim 45, to the extent that it depends upon claim 38, is of identical scope as claim 38, which already requires the inhibition of DPIV-mediated proteolysis.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982), *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 38-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 16-37 of copending Application No. 09/601,432. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '432 application anticipate the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 38-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 37-131 of copending Application No. 10/190,267. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the claims of the '267 application anticipate the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims 38, 39, 44-52, 54-57, 59, 60, 61, and 64 are rejected under 35 U.S.C. 103(a) as being obvious over the Deacon et al article or the Balkan et al abstract, each in view of the WO Patent Application '309 and further in view of Efendic et al. The Deacon et al article teaches potentiating the insulinotropic effect of GLP-1 by administering a DPIV inhibitor, valine-pyrrolidide. Administration is in vivo to a pig, and results in reduced proteolysis of GLP-1, reduced blood glucose, and increased glucose tolerance. See, e.g., the Abstract; Figure 1; and page 768, column 1. The Balkan et al abstract teaches improving the glucose tolerance of insulin resistant, glucose intolerant, obese Zucker rats by administering the DPP-IV inhibitor SDZ 272-070 (i.e. valine pyrrolidide). The Deacon et al article and the Balkan et al abstract do not disclose the use of DPIV inhibitors having a Ki and an EC_{50} as recited in claims 38, 39, and 47-50 or having the structure recited in instant claims 54-57, 59, 60, 61, and 64. The WO Patent Application '309 teaches administering DPIV inhibitors to treat human disease. The inhibitors are highly potent, with Ki values ranging into the nanomolar range or less, and are chemically stable. The DPIV inhibitors with the smallest Ki have the same structure as is set forth in Applicants' claims 54-57, 59, 60, 61, and 64. See, e.g., page 3, lines 10-21; page 4, lines 1-3; compounds 23, 38-40 and 97; and Table 9. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the DPIV inhibitors of the WO Patent Application '309 in the methods of the Deacon et al article or the Balkan et al abstract

because the DPIV inhibitors of the WO Patent Application '309 have the advantage of having a low Ki and of having chemical stability, which would permit the use of smaller dosages of the active agent, because the DPIV inhibitors of the WO Patent Application '309 are described as being generally useful as inhibitors of DPIV-mediated processes (see, e.g., the Abstract), and because the methods of the Deacon et al article and the Balkan et al abstract operate via a DPIV-mediated process. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to choose DPIV inhibitors from the WO Patent Application '309 for use in the methods of the Deacon et al article or the Balkan et al abstract so as to maximize their effectiveness in treating the intended disease and to minimize their unintended side effects, e.g., so as to minimize their EC_{50} for inhibiting glucose intolerance and to maximize their EC_{50} for causing immunosuppression. The Deacon et al article teaches administration of GLP-1 in combination with a DPIV inhibitor in pigs, which were chosen because of their resemblance to humans in terms of gastrointestinal physiology (see page 764, column 2, second full paragraph), and teaches that this may be a viable approach to the management of diabetes (see the Abstract), but does not explicitly teach co-administering GLP-1 and a DPIV inhibitor to treat Type II diabetes. The Balkan et al abstract teaches that administration of its DPP-IV inhibitor may be a useful tool in the treatment of NIDDM, but does not explicitly teach administering a DPP-IV inhibitor to treat Type II diabetes. Efendic et al teach that diabetes is characterized by impaired glucose metabolism manifesting itself among other things by elevated blood glucose levels, i.e that diabetic patients are glucose intolerant (see column 1, lines 19-21), and teach the administration of GLP-1 in order to treat type II diabetes (see, e.g., column 2, lines 37-49, and column 4, lines 47-67). It would have been obvious to one of ordinary skill in the art at the time

Applicants' invention was made to treat Type II diabetes using the combination of GLP-1 and a DPIV inhibitor suggested by the Deacon et al article as modified above by the WO Patent Application '309 or using a DPP-IV inhibitor suggested by the Balkan et al abstract as modified above by the WO Patent Application '309 to treat Type II diabetes, because the Deacon et al article and the Balkan et al abstract disclose that these may be viable approaches to the management of diabetes, because the Deacon et al article's in vivo pig model and the Balkan et al abstract's rat model are predictive of in vivo success in humans due to their resemblance to humans in terms of physiology, and because Efendic et al confirm that GLP-1 is useful in the treatment of Type II diabetes.

13. Claims 38, 39, 41, 44-63, 65, and 66 are rejected under 35 U.S.C. 103(a) as being obvious over the Deacon et al article or the Balkan et al abstract, each in view of the WO Patent Application '259 and further in view of Efendic et al. The Deacon et al article teaches potentiating the insulinotropic effect of GLP-1 by administering a DPIV inhibitor, valine-pyrrolidide. Administration is in vivo to a pig, and results in reduced proteolysis of GLP-1, reduced blood glucose, and increased glucose tolerance. See, e.g., the Abstract; Figure 1; and page 768, column 1. The Balkan et al abstract teaches improving the glucose tolerance of insulin resistant, glucose intolerant, obese Zucker rats by administering the DPP-IV inhibitor SDZ 272-070 (i.e. valine pyrrolidide). The Deacon et al article and the Balkan et al abstract do not disclose the use of DPIV inhibitors having a Ki and an EC_{50} as recited in claims 38, 39, and 47-50, having oral activity, or having the structure recited in instant claims 54-63, 65, and 66. The WO Patent Application '259 teaches inhibiting the enzymatic activity of DPIV in a mammal by administering a peptide compound. The peptides compounds are proteolyzed by DPIV in vivo

until a C-terminal dipeptide portion remains, which acts as an inhibitor of DPIV. The peptide compound is more stable in vivo than the C-terminal dipeptide portion. If the C-terminal dipeptide portion is chosen to be a dipeptide prolyl-boronic acid, then a potent and highly specific inhibitor having a Ki in the nanomolar range is ultimately released in vivo. Tetrapeptides comprising Ala-boroPro and Pro-boroPro as the C-terminal dipeptide portions are taught. As an alternative to the boroPro group, trifluoroalkyl ketone groups are taught. Administration can be oral. See, e.g., page 2, lines 15-32; page 3, line 1 - page 7, line 16; page 14, lines 10-12; page 14, line 34 - page 15, line 16; and page 21, line 15. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the DPIV inhibitors of the WO Patent Application '259 in the methods of the Deacon et al article or the Balkan et al abstract because the DPIV inhibitors of the WO Patent Application '259 have the advantage of having a low Ki and of having chemical stability, which would permit the use of smaller dosages of the active agent, because the DPIV inhibitors of the WO Patent Application '259 are described as being generally useful as inhibitors of DPIV-mediated processes (see, e.g., page 6, lines 4-10) and the methods of the Deacon et al article and the Balkan et al abstract operate via a DPIV-mediated process, and because the DPIV inhibitors of the WO Patent Application '259 can be administered orally, which is a more convenient and acceptable method of administration for the patient. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to choose DPIV inhibitors from the WO Patent Application '259 for use in the methods of the Deacon et al article or the Balkan et al abstract so as to maximize their effectiveness in treating the intended disease and to minimize their unintended side effects, e.g., so as to minimize their EC_{50} for inhibiting glucose

intolerance and to maximize their EC_{50} for causing immunosuppression. The Deacon et al article teaches administration of GLP-1 in combination with a DPIV inhibitor in pigs, which were chosen because of their resemblance to humans in terms of gastrointestinal physiology (see page 764, column 2, second full paragraph), and teaches that this may be a viable approach to the management of diabetes (see the Abstract), but does not explicitly teach co-administering GLP-1 and a DPIV inhibitor to treat Type II diabetes. The Balkan et al abstract teaches that administration of its DPP-IV inhibitor may be a useful tool in the treatment of NIDDM, but does not explicitly teach administering a DPP-IV inhibitor to treat Type II diabetes. Efendic et al teach that diabetes is characterized by impaired glucose metabolism manifesting itself among other things by elevated blood glucose levels, i.e. that diabetic patients are glucose intolerant (see column 1, lines 19-21), and teach the administration of GLP-1 in order to treat type II diabetes (see, e.g., column 2, lines 37-49, and column 4, lines 47-67). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat Type II diabetes using the combination of GLP-1 and a DPIV inhibitor suggested by the Deacon et al article as modified above by the WO Patent Application '259 or using a DPP-IV inhibitor suggested by the Balkan et al abstract as modified above by the WO Patent Application '259 to treat Type II diabetes, because the Deacon et al article and the Balkan et al abstract disclose that these may be viable approaches to the management of diabetes, because the Deacon et al article's in vivo pig model and the Balkan et al abstract's rat model are predictive of in vivo success in humans due to their resemblance to humans in terms of physiology, and because Efendic et al confirm that GLP-1 is useful in the treatment of Type II diabetes.

14. Claims 38-41, 44-52, 54-57, 59, 60, 63, and 66 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application '644. The WO Patent Application '644 teaches administering GLP-2 in combination with a DPP IV inhibitor such as Pro(boro)Pro in order to promote the growth of small and/or large intestine tissue in a mammal. Treatment of diabetes mellitus is also mentioned. The DPP IV inhibitor prevents proteolysis of GLP-2. See, e.g., page 3, lines 20-32, page 7, lines 15-22; page 9, line 17 - page 10, line 4; page 17, line 32; and Example 6. Because the same active agents are being administered to the same animals according to the same method steps, inherently metabolism of GLP-1, glucose metabolism, insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, hyperlipoproteinemia, and peptide hormone metabolism will be modified to the same extent in the method of the WO Patent Application '644 as is claimed by Applicants. With respect to instant claims 38-40 and 47-50, in view of the similarity in structure and function between the DPIV inhibitor of the WO Patent Application '644 and Applicants' claimed DPIV inhibitor, the EC50's and Ki for the DPIV inhibitor of the WO Patent Application '644 will inherently be the same as is recited in instant claims 38-40 and 47-50. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitor of the WO Patent Application '644 and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of the WO Patent Application '644. The WO Patent Application '644 discloses the treatment of diabetes mellitus, which inherently involves glucose intolerant subjects, but does not explicitly exemplify such treatment using GLP-2 in combination with a DPP IV inhibitor. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat

diabetes mellitus using a combination of GLP-2 and a DPP IV inhibitor because it is desirable to treat diabetes mellitus in patients and because the WO Patent Application '644 includes diabetes mellitus as a disease which can be treated with its GLP-2-containing compositions.

15. Claims 38-41, 44-52, 54-57, 59, 60, 63, and 66 are rejected under 35 U.S.C. 103(a) as being obvious over Drucker (U.S. Patent No. 5,952,301). Drucker is the U.S. equivalent of the WO Patent Application '644 applied above, is available a [illegible] laims under 35 U.S.C. 102(e) even should Applicants submit ar [illegible] under 35 U.S.C. 120 and 119(e), and renders Applicants' claims ol [illegible]

16. Claims 38-40 and 44-53 are rejected under 35 U.' [illegible] ıticipated by Villhauer. Villhauer teaches treating non-insulin-dependent diabetes, i.e. Type II diabetes, and increasing glucose tolerance by administering a DPIV inhibitor having the same structure as Applicants' page 9, line 7 - page 11, line 10. The inhibitors improve early insulin response to oral glucose challenges. Oral administration of the inhibitors is taught. See, e.g., the Abstract; column 9, lines 48-65; and column 10, lines 28-42. With respect to instant claims 38-40 and 47-50, in view of the similarity in structure and function between the DPIV inhibitor of Villhauer and Applicants' disclosed DPIV inhibitors, the EC50's and Ki for the DPIV inhibitors of Villhauer will inherently be the same as is recited in instant claims 38-40 and 47-50. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitors of Villhauer and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than the DPIV inhibitors of Villhauer. With respect to instant claim 40, because the same active agents are being administered to the same animals

according to the same method steps, inherently peptide hormone metabolism will be modified to the same extent in the method of Villhauer as is claimed by Applicants.

17. Claims 38-40 and 44-53 are rejected under 35 U.S.C. 102(b) as being anticipated by the German Patent 196 16 486. The German Patent '486 teaches using DP IV inhibitors to inhibit degradation of gastric inhibitory peptides and glucagon-like peptides, which effect can be used to reduce blood sugar levels and to treat diabetes mellitus. Inhibitors include alanyl pyrolidide, isoleucyl thiazolidide, and N-valyl prolyl, O-benzoyl hydroxyl amine, and they can be administered orally. See, e.g., pages 1-2; page 10, line 21 - page 11, line 1; and page 11, line 15; of the attached translation. In view of the similarity in structure and function between the DPIV inhibitors of the German Patent '486 and Applicants' disclosed and claimed DP IV inhibitors, the EC_{50} and K_i values for the DP IV inhibitors of the German Patent '486 will inherently be the same as those recited in the instant claims. Sufficient evidence of similarity is deemed to be present between the DP IV inhibitors of the German Patent '486 and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than those of the German Patent '486.

18. Applicant's arguments filed July 24, 2002 have been fully considered but they are not persuasive.

The rejection of claim 66 under 35 U.S.C. 112, second paragraph, is repeated in paragraph 6 above because there was no amendment to the claim to address this issue. The objection to claim 65 is repeated in paragraph 7 above because there was no amendment to the claim to address this issue. Claims 44 and 45 remain objected to as set forth in paragraph 8 above because no amendment instruction was found canceling these two claims.

The rejections based upon the Deacon et al article as the primary reference are maintained. The Deacon et al article remains prior art against the instant claims until Applicants have submitted an appropriate claim for priority which antedates the Deacon et al article. See paragraph 3 above.

The obviousness rejection based upon the WO Patent Application '644 is maintained. Applicants have not canceled the claims which were rejected upon the basis of obviousness over this reference.

The anticipation rejection based upon Villhauer is maintained. Animals with non-insulin-dependent diabetes mellitus are glucose intolerant, and Villhauer teaches treating such animals (see, e.g., the Abstract). Further, deletion of the -CN substituent from certain of the dependent claims does not mean that the broader independent claims no longer embrace the presence of such a substituent.

The anticipation rejection based upon the German Patent '486 is maintained. Animals with diabetes mellitus are glucose intolerant. Further, Applicants did not submit any evidence which would rebut the prima facie case of anticipation, e.g., which would show that the active agents of the German Patent '486 do not have the Ki recited in Applicants' claims.

15. The references crossed off of the Information Disclosure Statement filed March 4, 2002 are duplicate citations.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

April 22, 2003